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EXAMINER

BAKER, ANNE MARIE

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1632

DATE MAILED: 04/23/2002

29

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/963,288

Applicant(s)

NORSTEDT ET AL.

Examiner

Anne Baker

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 February 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,5,7-11,15,17,19-21,23-32,34-36,39-42,44-50,52 and 53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 34-36,41,42,46-48 and 50 is/are allowed.
- 6) ☒ Claim(s) 1,2,5,7-11,15-17,19-21,23-32,39,40,44,45,49,52 and 53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *detailed action*.

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DETAILED ACTION

The amendment filed February 7, 2002 (Paper No. 28) has been entered. Claims 1, 5, 8, 10, 15, 19, 27, 30, and 44 have been amended.

Accordingly, Claims 1, 2, 5, 7-11, 15-17, 19-21, 23-32, 34-36, 39-42, 44-50, 52, and 53 remain pending in the instant application.

The following rejections are reiterated or newly applied and constitute the complete set of rejections being applied to the instant application. Rejections and objections not reiterated from the previous office action are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-11, 16, 17, and 27-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims include new matter.

Claim 8 is directed to an expression vector comprising a structural gene encoding a desired protein or polypeptide and a promoter, wherein the vector further comprises **six enhancer elements**, and further **wherein at least one of the enhancer elements consists essentially of the nucleotide sequence TTCTGAGAA**. Claims 9-11, 16, and 17 depend from Claim 8.

Claim 27 is directed to an expression vector comprising a structural gene encoding a protein, a promoter, and at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA, wherein **the enhancer element is incorporated within the structural gene** by transfection. Claims 28 and 29 depend from Claim 27.

Claim 30 is directed to a DNA construct comprising a promoter, a structural gene, and at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA, wherein **the enhancer element is incorporated within the structural gene** by transfection. Claims 31-32 depend from Claim 30.

With regard to Claim 8, the claim recites six enhancer elements, only one of which is defined (“wherein at least one of the enhancer elements consists essentially of the nucleotide sequence TTCTGAGAA”). The other 5 enhancer elements are undefined and therefore encompass any and all enhancer elements. However, the specification does not contemplate using any enhancer element other than those comprising the nucleotide sequence TTCTGAGAA. Although a wide variety of enhancer elements are known in the art, the specification does not contemplate using other types of enhancer elements in combination with an enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA. Example 3 of the specification describes using reporter plasmids containing one to six copies of the 50 base pair SPI element fused to the TK promoter. The SPI element comprises the nucleotide sequence TTCTGAGAA. Example 3 is the only place in the specification where the use of six TTCTGAGAA-containing enhancer elements is described. Nowhere does the specification contemplate using enhancer elements other than those comprising the nucleotide sequence TTCTGAGAA. Furthermore, the specification does not contemplate using other types of enhancer elements in combination with an enhancer element comprising the nucleotide sequence TTCTGAGAA. Prior to the present amendment of Claim 8, all six enhancer elements were defined (although the particular

combination of the different types of elements also constituted new matter). Applicants have not pointed to any support in the specification for the amendment to Claim 8.

With regard to Claims 27 and 30, the claims recite that the enhancer element is incorporated **within** the structural gene. However, the specification does not contemplate or describe expression vectors or DNA constructs comprising an enhancer element incorporated **within** a structural gene. The specification only describes constructs where the enhancer element was placed upstream from the promoter. For example, in Example 5, at page 4 of the specification, six copies of the SPI element were introduced upstream of a strong CMV promoter driving expression of CAT cDNA. Furthermore, the specification does not describe the function of constructs or expression vectors that have the enhancer element incorporated within the structural gene. The specification only teaches the function of the enhancer element when it is located upstream of the promoter. Moreover, it is noted that incorporating the enhancer within the structural gene would disrupt the coding sequence of the gene and thereby interfere with expression of the gene instead of enhancing expression of the gene. Applicants have not pointed to any support for the amendment to Claims 27 and 30.

Thus, the claimed invention is not adequately described in the specification and the amendment introduces new matter into the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 5, 7, 10, 15, 19-21, 23-27, 30, 39, 40, 44, 45, 49, 52, and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 39, 40, 51, and 52 are indefinite because the claims recite steps (a), (b), and (c) but the claim language does not indicate whether the method “comprises” or “consists of” these method steps.

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The claim language “the method comprising the steps of” has been removed. Furthermore, in step (a) which has been amended to recite the arrangement of the genetic elements, it is unclear if the promoter is operably linked to the structural gene.

Claims 5, 7, 15, 23-26, and 53 are indefinite in their recitation of “a DNA construct transfected into the genome of a eukaryotic host cell” because a DNA construct is transfected into a **cell**, not into a **genome**. Rather, a DNA construct is **incorporated** into a genome. Use of claim language reciting “a DNA construct incorporated into the genome of a eukaryotic host cell” is suggested.

Claim 10 is indefinite in its recitation of “wherein the enhancer element comprises at least one copy of the nucleotide sequence SEQ ID NO: 1” because “the enhancer element” has ambiguous antecedent basis. Since the claim recites six enhancer elements and each can be different from all the others, it is unclear to which enhancer element the claim is referring.

Claims 19-21 and 49 are indefinite in their recitation of “providing the DNA construct with the nucleotide sequence consisting of TTCTGAGAA upstream of the promoter” in part (b) because “providing” is not sufficient to incorporate the enhancer element into the DNA construct upstream of the promoter. Use of claim language reciting “incorporating a nucleotide sequence consisting of TTCTGAGAA into the DNA construct upstream of the promoter” is suggested.

Claims 19-21 and 49 are indefinite because the claims recite steps (a), (b), (c), and (d), but the claim language does not indicate whether the method “comprises” or “consists of” these method steps. The claim language “the method comprising” has been removed. Furthermore, in step (a) which has been amended to recite a new step, it is unclear if the promoter is operably linked to the structural gene. Operable linkage is essential to the operability of the invention.

Claims 19-21 and 49 are indefinite in their recitation of “the DNA construct” in steps (c) and (d) and at the end of Claim 49 because the phrase has ambiguous antecedent basis. Claim 19 has been amended to add a new step (a) which recites “a DNA construct comprising a structural gene and a

promoter upstream of the structural gene.” In step (b) a new DNA construct is produced which comprises a promoter, structural gene and enhancer. Thus, it is unclear which DNA construct is used in step (c) for transfection. Since there is no literal antecedent basis for “the DNA construct” referred to in steps (c) and (d) other than the DNA construct of step (a), the later steps appear to be using the construct that does not comprise the enhancer element.

Claims 27 and 30 are indefinite in their recitation of “wherein the enhancer element is incorporated within the structural gene by transfection” because **cells** are transfected. Genes cannot be transfected. Furthermore, even if the enhancer element was transfected into a cell, it would not be incorporated into the expression vector. Thus, it is unclear how transfection of an enhancer element alone would result in incorporation of the enhancer element “within the structural gene.” Furthermore, the structural gene is within the expression vector and it is unclear where the expression vector is during said transfection. Furthermore, it is unclear where within the structural gene the enhancer element is incorporated. The claim encompasses having the enhancer element disrupting coding sequences. The placement of the enhancer element is essential to the operability of the invention.

Claims 44 and 45 are indefinite because it is unclear if the promoter is operably linked to the structural gene. The claims have been amended to recite the arrangement of the genetic elements, but it is unclear if the promoter recited in the claim is the promoter that drives expression of the structural gene or some other promoter that is not operably linked to the structural gene. Operable linkage of a promoter to the structural gene is essential to the operability of the invention. Use of claim language reciting “[a]n isolated DNA construct comprising a promoter operably linked to a structural gene, and six repeats of an enhancer element upstream from said promoter, wherein the enhancer element consists essentially of the sequence TTCTGAGAA” is suggested.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 27-32 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Lindquester et al. (1989) for reasons of record advanced in the Office Action mailed 4/26/00 (Paper No. 16), in the Office Action mailed 11/22/00 (Paper No. 19), and in the Office Action mailed 8/15/01 (Paper No. 27).

The claims are directed to an expression vector comprising at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA, an isolated eukaryotic host cell containing the expression vector, and a DNA construct comprising a promoter, a structural gene and at least one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA.

At page 9, paragraph 1 of the response, Applicants argue that Lindquester et al. does not provide a teaching, suggestion or recognition of the ability of the nucleotide sequence to act as an enhancer element. Applicants arguments are not unlike those presented earlier. As discussed at page 6 of the Office Action of Paper No. 27 (mailed 8/15/01), Lindquester et al. need not disclose the function of the sequence because the claims are directed to compositions that include this sequence. The function of the element is an inherent property of the composition. See MPEP 2112.01. When the structure recited in a reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent. Thus, the function of the enhancer element is considered an inherent property of the element.

At page 9, paragraph 1 of the response, Applicants argue that there is no teaching or suggestion to one of skill in the art to produce either an expression vector or DNA construct as recited in claims 27 and 30. However, the stated motivation for producing the expression vector, as set forth at page 8 of the Office Action of Paper No. 16 (mailed 4/26/00), is to produce the tropomyosin protein in culture and does

not rely on any recognition that the element contained in the gene is an enhancer element. Furthermore, the rejection stated that one would have anticipated a reasonable expectation of success for making the expression vector and host cell comprising the expression vector because only standard molecular biology techniques are required to make such compositions. Applicants have not addressed the stated motivation for producing the claimed compositions.

At pages 8-9 of the response, Applicants repeatedly argue that Lindquester et al. does not provide an enabling disclosure for incorporating the enhancer element within the structural gene by transfection. Again it is noted that the claims are directed to compositions, not methods, and thus any product-by-process type language is only a limitation for the claimed composition by the structure that it implies. In the instant case, the composition disclosed by Lindquester et al. meets all the structural limitations of the claimed compositions. Furthermore, as noted above, the claim language relating to incorporation of the enhancer element within a gene **by transfection** is indefinite and subject to a rejection under 35 U.S.C. 112, second paragraph. It is further noted that once the nucleotide sequence TTCTGAGAA is incorporated into an expression vector or DNA construct it is necessarily flanked by other nucleotide sequences and thus, the claim language reciting “[a]n expression vector comprising ... one enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA” necessarily requires that the enhancer element will be flanked by other nucleotide sequences. Thus, the composition disclosed by Lindquester et al. meets all the structural limitations of the claims.

The rejection of Claims 19, 20, and 49 under 35 U.S.C. 102(b) as being anticipated by Yoon et al. (1990) is withdrawn in view of the amendment to the claims which requires a separate step where the nucleotide sequence consisting of TTCTGAGAA is introduced into a DNA construct comprising a structural gene and a promoter.

Conclusion

Claims 34-36, 41, 42, 46-48, and 50 are allowable. The prior art of record does not disclose or reasonably suggest using an enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA or multiple copies of the enhancer element consisting essentially of the nucleotide sequence TTCTGAGAA in the claimed method of enhancing the transcription of a gene.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Baker whose telephone number is (703) 306-9155. The examiner can normally be reached Monday through Thursday and alternate Fridays from 10:00 AM to 7:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Anne-Marie Baker, Ph.D.

Anne-Marie Baker
ANNE-MARIE BAKER
PATENT EXAMINER